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WALTER BRADFORD CANNON

1871—1945

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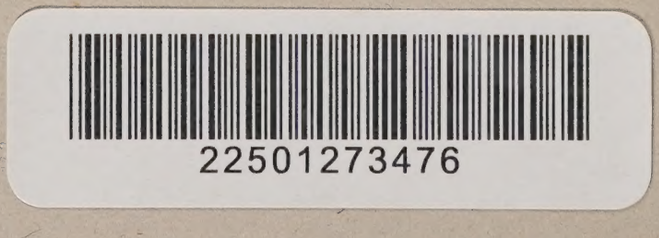
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Walter B. Cannon

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WALTER BRADFORD CANNON

1871–1945

THE work as a physiologist of Walter Bradford Cannon, who died on 2 October 1945, belongs to a tradition which may possibly have passed already the peak of its influence. Its followers have been concerned with the systematic description and provisional interpretation of the functions of living beings as seen, for the most part, in vertebrate animals. Their ultimate aim has been to create a physiology of man, as one of the foundations of medical science, though their immediate objective has more often been the analysis of animal functions more accessible to experiment. Their methods have had a background of human and vertebrate anatomy, and they have called in aid only the more readily available teachings and methods of physics and chemistry, with such instrumental aids as their own ingenuity could devise from these. This tradition goes back to William Harvey, but its proximate origin, or revival, in the mid-nineteenth century can be traced to the laboratories of Claude Bernard in Paris and Carl Ludwig in Leipzig; and the large contribution which has been made by the English-speaking countries to this stage in the development of physiology has been due, in the main, to men who had studied under one or other of these leaders, or received the tradition as handed down by those who were thus directly their pupils. Cannon received it with more than usual directness, for one who was a contemporary of men still living and active; for he began his work early enough to be an immediate pupil of H. P. Bowditch, who had learned his physiology with Carl Ludwig. Cannon, thus, as a physiologist, claimed Ludwig as 'grandfather', and all his life's work endorsed his title to membership of that great family. He was one of the physiologists still concerned with the integrated functions of organs and systems, and he investigated these with the simple macroscopic technique which his own inventive faculty would provide, and which his remarkable manual dexterity would enable him to undertake. His equipment in the more fundamental sciences was little more than that which the ordinary medical curriculum would furnish for an able and eager student. Like many of his predecessors and contemporaries, he was content, therefore, to leave to those who would come after him, or to his own immediate colleagues, the development of a finer physico-chemical analysis of the functions of the individual living cell and its components. Yet, as was shown by his use in his first important research of the then recently discovered X-rays, Cannon was always alert to apply new experimental resources within the range of the physiological methods of which he was a master. With that phase of the development of what he himself has called 'synthetic or integrative physiology', and especially with the American contribution to it, Cannon's name will always be honourably associated.

Cannon could proudly trace his lineage to pioneering ancestry on both sides. His mother's surname, Denio, came from a French-Canadian trapper, Jacques de Noyon, who in 1704 had married the daughter of a British colonist of Deerfield, Massachusetts; one of their offspring, René de Noyon, having had his name conveniently anglicized to 'Aaron Denio'. His father's ancestors were immigrants from Ulster who landed in Boston in 1718; and again the original name, Carnahan, had become modified to Cannon, apparently to simplify its spelling. Both these families had contributed early settlers to the great westerly migration. Cannon tells of a great-grandmother on his father's side who walked beside a covered wagon from Blandford, Massachusetts, to Aurora, Ohio, rode through a winter night on an errand of mercy, spent her spare time at the loom, bore eight children and lived to be ninety. Of parents with such ancestry Walter Cannon was born on 19 October 1871, at Prairie du Chien, Wisconsin, on the upper Mississippi. He was later to acquire an added interest in his birthplace, when he discovered that it was built on the site once occupied by Fort Crawford, where William Beaumont, an American army surgeon, had laid the foundations of the physiology of gastric digestion, using the opportunity presented by the stomach-wound of a Canadian, Alexis St Martin. Cannon's father, a railroad official with a turn for invention, taught the boy to make his own toys and gave him the freedom of a well-found workshop. His mother, who had been a schoolteacher, died early, when her son was ten years old. He went to the public primary and grammar schools in Milwaukee and St Paul, Minnesota, and later to the High School at St Paul. The course was interrupted by two years in a railroad office, from fourteen to sixteen, apparently because his father thought he had been idling; and thus, though he went through the High School course in less than standard time, he was twenty years of age when it was finished. Then to Harvard, which opened a new world of ideas, and brought stimulating contacts with C. B. Davenport, G. H. Parker and William James.

After graduation from Harvard College, Cannon had four years more in the Medical School, supporting himself throughout these student years by scholarships and by outside work. He became M.D. in 1900, at the age of twenty-nine, and had then a choice between continuing an instructorship in zoology at Harvard College and beginning one in physiology under Henry P. Bowditch, in the Harvard Medical School in Boston. He chose the latter, and began an association with that Department of Physiology which was to last till his retirement from its chair forty-two years later.

Cannon's experience of research, however, had begun even before he entered upon his medical course, when he assisted Professor Davenport, at Harvard College, with some experiments on the phototaxis of minute organisms. In his first year in the Medical School the discovery of X-rays by Röntgen, and their application in surgery to render the bones visible, were comparative novelties. Encouraged by Bowditch, he interested himself in watching, by means of X-rays and a fluorescent screen, the shadow of a metal ball passing down the oesophagus of a goose which had been induced to swallow it. Then it occurred to them that a meal could be made to cast such a shadow, and to show the changing shape of

the stomach or other part of the alimentary canal through which it was passing, if it was suitably mixed with a substance opaque to the X-rays. Cannon tells us that he found that several insoluble salts of heavy metals could be used for this purpose, including barium sulphate as well as bismuth subnitrate. He blames himself for mentioning only the latter in his published description of the experiments, so that it was left for others to discover, much later, the suitability and, incidentally, the superiority of barium sulphate for such uses in practical medicine. Cannon's original use of this method kept him occupied for many years with a detailed description of the whole course of the passage of a suitably compounded meal through the body of the normal, unnarcotized cat. During swallowing, digestion, absorption and ultimate elimination of residue, he could follow on the screen the movements and segmentation of the opaque mass, and deduce the contractile activities of the successive divisions of the alimentary canal. In so doing, he had not only added, thus early in his career, an important chapter to normal physiology; he had also given to medicine and surgery one of the most important items in a modern diagnostic equipment.

A glance at the record of his scientific publications might suggest that Cannon's interest, during his many years of activity in physiological research, was attracted to a succession of problems having no clear relation to one another. A study of the papers themselves, however, shows him as led from one field to another by clues which presented themselves naturally, in the course of his own observations. Thus, in his earliest series of important researches, when he was first observing the movements of the stomach and bowels by X-rays, he noticed, first as a detrimental break in the continuity of his observations, that the movements he was studying were apt to suffer a sudden diminution, or a complete suppression, and that he would have to wait a variable time for their resumption. He found then that such a period of inhibition was associated with an emotional reaction to a sudden noise, or to any stimulus which caused the animal to exhibit fright or anger. His curiosity was thus aroused in the visceral concomitants of emotional states, and, when opportunity served, he embarked on an investigation of the nervous and other influences responsible for their production. An inspection of the bibliographic list attached to this notice will show, however, that Cannon was by no means in a hurry to move from the first, abundantly fruitful field of his researches. In one of his first papers, on the movements of the stomach as seen by X-rays, he tells us that the suggestion that he should explore the possibility of such a method was made to him by Bowditch as early as the autumn of 1896; and we find him still publishing developments of research on these lines as late as 1911. By 1906, however, Cannon, who had now succeeded Bowditch in the Chair of Physiology at the Harvard Medical School, had begun to study the effects on visceral movements of dividing the splanchnic and vagus nerves. At this time, and in the years immediately following, the action of adrenaline and its relation to the effects of sympathetic nerves, together with the conditions governing the output of this hormone from the adrenal glands, formed a centre of growing interest for a number of physiologists. This fluctuating output of adrenaline might obviously be a factor in the control of the visceral

activities which Cannon had studied so long. In 1911 we find him publishing a paper with De la Paz on 'The emotional stimulation of adrenal secretion', and this was followed, in the next year, by papers with various co-workers on the effects of asphyxia, hyperpnoea and sensory stimulation on adrenal secretion, on emotional glycosuria, and on the effect of splanchnic stimulation on muscular fatigue, as well as by others still directly concerned with the original problem of co-ordinated movements of the viscera. Thus Cannon passed naturally into the second main phase of his career as an investigator, in which he dealt with the general physiological functions of the nerves of the sympathetic system and of adrenaline, with the influences determining the rate at which the latter substance is secreted into the blood, and particularly with the functional significance of its effects in preparing the body for the emergency of combat or flight. With a growing band of keen collaborators he explored this group of problems in all its aspects over a period covering about a decade, with an interruption of some two years by abnormal duties and distractions arising from the war in Europe. There resulted not only a series of publications in specialist journals, culminating in 1914 with a general survey of 'The function of the adrenal medulla in pain and the major emotions', but a comprehensive review, dealing with the whole course of this investigation and the general conclusions which emerged. This was presented by Cannon in a narrative and explanatory form, suitable even for readers with no special physiological training, in a book with the title, *Bodily changes in pain, hunger, fear and rage.* This had a wide circulation and established his reputation as an attractive and vivid expositor, to a wider public, of a group of practical ideas arising from his own researches and those of his contemporaries. His studies of this mechanism of sympathetic and adrenal control led Cannon to consider next the more general system of natural adjustments to varying demands, through which the normal body keeps approximately constant the conditions which determine its vital efficiency, such as the content of sugar and of inorganic ions, and therewith the slight alkalinity of the blood, restoring them rapidly to their accustomed levels after functional fluctuations. The general conception had been a central part of physiological teaching since Claude Bernard wrote of 'the constancy of the internal environment'; but Cannon had begun to explore its possibilities to new purpose and from new angles, when the war diverted his activities into special channels. Later he was to embody the results of this group of his observations and thoughts in another book for the general reader, more widely philosophical in its outlook than the earlier one, and entitled *The wisdom of the body*—a title which Cannon adopted by quotation from E. H. Starling's Harveian Oration.

The United States had already entered the war of 1914–1918 when Cannon went to France, in May 1917, as a member of the Harvard Hospital Unit, attached to the British Army in advance of the arrival of American troops in the field. He was eager to take the opportunity to apply his knowledge and his technique of research to the problem presented by the condition, or group of conditions, which the surgeons termed 'shock'. He was unwilling, therefore, to stay at a base hospital, and keen to see for himself and to investigate cases of

wound shock at a Casualty Clearing Station. This opportunity he found at Bethune, with Colonel (later Sir) Cuthbert Wallace and other surgeons serving with the British Army. Here he worked cheerfully, under conditions of frequent stress and difficulty, for some six months; incidentally he made a number of new friendships and was to become a very successful chairman, at a later stage, of a Medical Research Committee of the Allies meeting in Paris. Meanwhile his work at Bethune had led him to ideas concerning the nature of shock and the relation to it of a fall of the alkali-reserve of the blood plasma, which he regarded as a cause rather than an effect of the deficient circulation; and he desired to put these ideas to the test of experiment. He came to England, accordingly, in November 1917 and worked with the late Sir William Bayliss, becoming with him a member of a committee of workers with like interests then meeting in London, which included also Sherrington, Starling and A. N. Richards (from Philadelphia), as well as the writer of this notice. The free interchange of ideas and the challenging conflict of experimental findings among this group were not without dramatic and even humorous incident; but ultimately Bayliss and Cannon were convinced that, so far as a chemical factor was concerned in the genesis of shock as they produced it experimentally, and as Cannon had seen it in the field, this factor was the release of a directly toxic agent, rather than a primary acidosis; and Cannon's book on *Traumatic shock*, written after the war, adopted this interpretation. It is unlikely that any of those concerned in this effort to find a rapid solution for a complex and ill-defined problem, in order to meet an immediate emergency of war, expected that the validity of their conclusions would have even a normal permanence; but, as Cannon himself claimed in his last book, *The way of an investigator*, published shortly before his death, 'experiences in researches on shock during World War I could be put to use in World War II'.

With the beginning of the arrival of the American Army in France Cannon took up appointment as director of a central laboratory for research on shock and other medical problems at Dijon. After the armistice he was soon back in his own laboratory, picking up the dropped threads of his researches on the sympathetic-adrenal system. One of the developments of these made full demands on his unusually fine technique of surgical experiment, involving the entire removal of both the main sympathetic nerve-chains and extirpation of the suprarenal medulla. The use of the denervated heart as a sensitive indicator of the release of adrenaline led directly to the studies forming the third and last of the main phases of Cannon's research career. Late in 1921 he published, with Uridil, a paper describing the acceleration of such a heart when the hepatic nerves were stimulated, even after the adrenal glands had been extirpated. Similar effects at a distance, transmitted by the circulation, were later recognized by Cannon and his colleagues as the result of stimulating other sympathetic nerves; and it seems clear that, at the time when he published his first observation of this kind, he had been not far from a discovery which had, in fact, been made with a more simple and direct method by Otto Loewi, only a few months earlier. This was the transmission of the peripheral effects of involuntary nerves

by chemical mediators, which had been foreseen in principle by T. R. Elliott as early as 1904.

Cannon and his co-workers, during the remainder of his working life as an investigator, were to make a notable contribution to the rapid accumulation of evidence for such chemical transmission, to which many workers in different countries contributed. It was natural that the interest of his laboratory should be centred, for the first part of this period, on that aspect of the problem which concerned the true sympathetic system and its chemical transmitter. Cannon's own evidence appeared to him to lead to the conclusion that this sympathetic transmitter was not adrenaline itself, but an apparently related body, which he termed 'sympathin'. The position was rather complicated by the fact that Cannon's evidence was all based on the effects of this transmitter as it escaped naturally into the circulating blood from the point of its release, and that, according to Cannon's own view, it should by then have combined with a receptive substance 'E', determining a previously ambivalent activity in the direction of an augmentor effect. Evidence of other kinds has been advanced independently, however, and some of it quite recently, in support of Cannon's view that the essential sympathetic transmitter, his 'sympathin', may be a closely related base rather than adrenaline itself; and, whatever may be the final conclusion, Cannon with his co-workers continued over a period of many years to enrich physiology with a body of experimental observations of great elegance and independent interest, apart from the fact that Cannon was able to use them for a characteristically tenacious and resourceful defence of his own conviction. In the latter years of this third period Cannon's laboratory, and his close collaborator Rosenblueth in particular, contributed also to the exploration of a then newly revealed intervention of acetylcholine in the transmission of the excitatory process at ganglionic synapses and voluntary motor nerve endings. Cannon, in due course, once again did his fellow physiologists the important service of producing a summary and reasoned survey of the contributions made by himself and his colleagues, and many of those made by his contemporaries, to this whole story of chemical transmission, in the form of a book on *Autonomic neuro-effector systems*, the responsible authorship in this case being shared with him by Rosenblueth.

For almost exactly fifty years to the date of his retirement, as he himself noted with satisfaction, Cannon had been associated with Harvard University and its Medical School. Through all but the first few years of that period his predominant interest and concern had been with research in physiology. He had great qualities also as a teacher, and faithfully used them; he was proud of his contribution to the training of men for the high duties of medical practice. He certainly had good gifts, also, of administration, and it is not surprising that, as he himself records, he was pressed on more than one occasion to accept premier administrative positions at important medical schools. These latter temptations, however, he firmly and wisely resisted. There were others who could administer; the duty for which he felt qualified and which he supremely desired to undertake was that of research in his own chosen field, and the training

of those who should follow him there. Like J. J. Abel, his senior by fourteen years and a direct pupil of Carl Ludwig, Cannon, a 'grandson' in physiology of that great leader, presented to his contemporaries a shining example of a life devoted to the increase of knowledge for its own sake in his own chosen department of medical science, without thought of personal advancement or reward.

Cannon's conviction, however, that his best service to science and medicine would be rendered through research with his own hands and brain and those of his immediate colleagues, did not make him a cloistered devotee, or create in him any trace of aloofness from the wider interests of his colleagues, or of mankind at large. When any social campaign had enlisted his sympathy, his natural reaction was to support it actively, and in a chapter on 'Being a citizen' in his last book, he tells of some of the causes for which he had felt thus impelled to work, or to fight, in the course of his career. The list is so characteristic of the man, with his instinctive and impulsive reaction against anything which seemed to him to involve cruelty, tyranny, or stupid prejudice, that it must be cited, if only to note the order in which he mentions the crusades in which his sense of justice involved him. 'I am grateful', he writes, 'that fortunate conditions gave me opportunity to test democratic methods by opposing the efforts of anti-vivisectionists at destroying freedom of medical investigation; to attempt aiding republican forces in Spain and in China as they struggled against oppressors; and to promote deeper sympathy between the Americans and the Russians as they look forward to a better world.' Any one who knew Cannon well and enjoyed the privilege of his friendship must have felt that, in his whole outlook on life, and in the traditions and ideals on which he consciously based it, he was as essentially American as any of the ancestral line of pioneers of which he came. One felt that the great heart of America was beating in him, and that it had found embodiment in a brave and generous and sensitive personality.

Cannon married as soon as his medical course was finished, his bride being Cornelia James, who had been a fellow student with him in High School at St Paul, Minnesota. It was to be a marriage of perfect, lifelong sympathy, intimate understanding and sharing of aims. Mrs Cannon developed, in due course, her own activities and interests, as author of several accomplished mid-western novels and a champion, like her husband, of many efforts for the common benefit. From middle life, when Cannon had become professor, and thence to the end, their home was an attractive, old, wooden house of 'colonial' type in Cambridge, Mass. There, soon after the earlier world war, a fortunate guest encountered them, with Cannon's two sisters, engaged in social and educational duties, and with a lively and talented young family of a son and four daughters; and found himself welcomed to a household glowing with happiness and affection, and resounding with friendly chaff and merriment. Cannon himself relates that one of these daughters, in response to a little school-friend's boast that *her* father was a doctor, confessed that hers was 'only a father'; and it is certainly true that any one who had not seen Cannon as a father had missed a very important and attractive side of his character.

Several citations have been made already from Cannon's last book, a charmingly discursive mixture of autobiography, gossip, confession and testimony, with a style so like his conversation that a friend can almost hear the voice as he reads. In the chapter on 'Fitness for the enterprise' he gives high rank to vigorous health among the qualifications of an investigator, though he notes exceptions. In the earlier half of his life he must himself have been unusually well endowed in this respect. He was never conspicuous in competitive sports, but on his wedding tour he and his wife made a strenuous first ascent of a peak in the Rocky Mountains, which was named Mount Cannon to commemorate their achievement. Both continued to value the recreation to be obtained from vigorous walking in the wild. Towards the middle years, however, Cannon's health began to be troubled with tiresome allergies. When he came to Europe in 1917 he told us that he had acquired a specific and extreme sensitiveness to the guinea-pig, which had imposed limits on his research programme; and later he became sensitive to other and less easily avoided allergens, and suffered from loss of rest in consequence. Later still came the threatening discovery of a slowly malignant condition, which never thereafter left him, though its progress was less rapid than his friends and advisers had feared. He hardly mentioned it, but it is known that he suspected, perhaps rightly, that this trouble was a late result of the unheeding exposure of himself in his early experiments with X-rays, at a time when there was no thought that this might have dangerous consequences. However that may be, it was entirely characteristic of Cannon's quiet courage that he just went on with his work, though his rest was thus broken and his strength slowly undermined, during many of the years of his greatest productivity in research and of his most effective activity as a 'citizen'; and it was likewise characteristic of him that, when the end of his life was not far away, he still wrote of the gift of physical strength and health as one of the chief factors of success, in the career which he had chosen from the first and had followed with such unwavering devotion.

Of many honours which came to Cannon, in his own and other countries, it is fitting to make special mention here of his election in 1939 to the Foreign Membership of the Royal Society. He had given the Society's Croonian Lecture on 'The physical basis of thirst', in 1918, while he was still in Europe on war service. At the end of that war his services to this country and its army were recognized by the award of the C.B., while his own country gave him the Distinguished Service Medal. In 1942, on the death of Professor L. J. Henderson, he became the Foreign Secretary of the National Academy of Sciences of Washington, and, before death intervened, he had shown himself eager to collaborate with the Foreign Secretary of the Royal Society, and with representative scientists of other countries as it became possible to renew such contacts, in preparing for the revival of the International Scientific Unions and for any co-ordinated action which might contribute to the rebuilding of an international community in science.

H. H. Dale

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